

REMARKS

This Amendment serves as the submission accompanying Applicants' Request for Continued Examination (RCE) filed pursuant to 37 C.F.R. § 1.114. By final Office Action mailed April 12, 2005, pending claims 1, 33 and 34 stood rejected, reconsideration of which is respectfully requested in view of the above amendments and the following remarks. Claim 1 has been amended. Claims 1, 33 and 34 are now pending.

Claim Amendments

By way of this Amendment, Applicants have amended claim 1 to recite an additional step, namely, a step of "selecting a second fluid having a known viscosity" and to specify that "the second fluid is selected for achieving a desired flow rate at the interface between the fluid sample and the second fluid". Support for these amendments may be found generally throughout the specification, and, in particular, in the Abstract and in paragraphs [0009] and [0013] of the specification. Applicants submit that no new matter has been added by way of these amendments.

Rejection Under 35 U.S.C. § 112

Claims 1 and 33-34 stand rejected under 35 U.S.C. § 112, first paragraph, due to the inclusion of the terminology "laminar flow", which the Examiner asserts lacks adequate written description. Applicants respectfully disagree. The methods disclosed and claimed in the present application apply to microfluidic structures. As one of ordinary skill in the art would appreciate, and as disclosed in U.S. Patent Application No. 09/428,807 (incorporated by reference in paragraph [0001] of the present application) and U.S. Patent No. 5,948,684 (incorporated by reference in paragraph [0011] of the present application), fluid flow within microfluidic structures is laminar. Accordingly, Applicants submit that the pending claims satisfy the first paragraph requirements of §112 and request that this ground of rejection be withdrawn.

Rejections Under 35 U.S.C. § 102(e)

Claims 1 and 33-34 remain rejected under 35 U.S.C. § 102(e) as anticipated by Vigh et al. (U.S. Patent No. 6,511,850) or Weigl et al. (U.S. Patent No. 6,454,945) for the reasons set forth in the prior Office Actions and for the reasons set forth on pages 2-3 of the present Office Action. For the following reasons, Applicants respectfully disagree with the Examiner's application of Vigh and Weigl and submit that neither of such references anticipate the pending claims, as amended.

The claimed invention is directed to a method of controlling the flow rate of a fluid sample flowing through a microfluidic channel comprising three steps: (1) selecting a second fluid having a known viscosity; (2) sheathing the fluid sample within a center region of the second fluid flowing through the microfluidic channel; and (3) flowing the fluid sample and the second fluid through the microfluidic channel in laminar flow. In addition, the claimed method (*i.e.*, the foregoing three steps) comprises four characteristics: (1) the second fluid completely surrounds, and is in contact with, the fluid sample at an interface between the second fluid and the fluid sample; (2) the flow rate of the fluid sample is constant across the center region; (3) the flow rate of the fluid sample is substantially equal to the flow rate of the second fluid at the interface between the second fluid and the fluid sample; and (4) the second fluid is selected for achieving a desired flow rate at the interface between the fluid sample and the second fluid.

Neither Vigh nor Weigl disclose a method comprising each of the foregoing three steps and each of the foregoing four characteristics.

Vigh

Vigh discloses various pneumatic nebulizer interface devices for converting a sample stream into an aerosol in which a sample stream is combined with a sheath fluid stream to produce a combined fluid flow having a combined flow rate that matches the self-aspiration rate of the pneumatic nebulizer interface. As disclosed at column 1, lines 21-43, the devices ensure that the combined flow rate matches the self-aspiration rate without substantially altering the original feed rate of the sample stream by automatically self-adjusting the feed rate of the sheath fluid stream. In other words, in the disclosed devices, the flow rate of the sample stream

remains constant and the flow rate of the sheath fluid stream varies such that the sum of the sheath fluid flow and the sample fluid flow matches the self-aspiration rate of the nebulizer (*see, e.g.,* column 8, lines 34-42). Accordingly, the disclosed devices are specifically configured to provide for variability between the flow rates of the sample stream and the sheath fluid stream.

The Examiner notes that Vigh teaches that the flow resistance of the sheath fluid stream inlet is substantially negligible with respect to the flow resistance of the sample stream inlet (*see, e.g.,* (i) column 2, lines 9-23, (ii) Figure 1 and the corresponding description of such Figure at column 7, line 49, through column 9, line 14, and (iii) claim 22) and concludes that, consequently, the two fluids would flow at the same rate. Applicants disagree with this interpretation. The flow rates of the sample stream and the sheath fluid stream are controlled by the self-aspiration rate of (or amount of suction exerted by) the nebulizer. As the amount of suction exerted by the nebulizer increases, the combined flow rate of the sample stream and sheath fluid stream increases. In order to ensure that the sample stream is not subjected to changes in flow rate (which would result in band dispersion or broadening in the sample stream), the devices are configured such that the flow resistance of the sheath fluid stream inlet is substantially negligible with respect to the flow resistance of the sample stream inlet. In other words, the flow resistance of the sample stream inlet is much greater than the flow resistance of the sheath fluid stream inlet. *See, e.g.,* column 8, lines 43-67. In this way, the devices provide for the flow rate of the sheath fluid stream to increase first to compensate for any increases in the amount of suction exerted by the nebulizer.

Contrary to the Examiner's assertion, Vigh contains no disclosure regarding the relationship between the flow rates of the two fluids at the interface between the two fluids. Nor does Vigh contain any disclosure regarding the selection of a particular sheath fluid in order to influence the interaction between the two fluids at the interface between the two fluids. Accordingly, Applicants submit that Vigh does not disclose a method comprising step (1) or characteristics (2), (3) or (4) of the claimed method.

Weigl

Weigl discloses various systems and methods for extracting desired particles from a sample stream containing desired and undesired particles by flowing a sample stream and an

extraction stream through a microfluidic channel in parallel laminar flow for a sufficient period of time to allow differential transport of the desired particles from the sample stream into the extraction stream. As noted by the Examiner, Weigl discloses at, for example, column 7, line 38, that such fluid streams may have equal flow rates. In other words, in the passages cited by the Examiner, Weigl merely discloses that two fluid streams flowing side-by-side may have equal flow rates.

Contrary to the Examiner's assertion, such disclosure does not relate to the flow rates of a first fluid sheathed within a second fluid. In fact, although Weigl does note that various sheathing devices may be combined with the disclosed extraction apparatus to facilitate detection of the desired particles (*see* (i) column 15, line 11, through column 16, line 27, and (ii) Figure 22 and the corresponding description of such Figure at column 44, lines 14-59), Weigl further discloses at column 44, lines 52-54, that in an embodiment utilizing such a sheathing device, the center (or sheathed fluid) is "preferably at a lower ... speed than the sheath fluid". Furthermore, Applicants note that Weigl contains no disclosure regarding either (1) selecting a sheath fluid having a known viscosity for achieving a desired flow rate at the interface between the sheath fluid and the center (or sheathed) fluid, or (2) achieving a constant flow rate of the center (or sheathed) fluid across the center fluid.

Accordingly, Applicants submit that Weigl does not disclose a method comprising step (1) or characteristics (2), (3) or (4) of the claimed method.

Accordingly, in view of the foregoing, Applicants submit that neither of the foregoing references disclose every element of pending independent claim 1, as amended, nor do either of such references contain any teaching or suggestion to modify the methods disclosed therein in order to produce a method comprising every element of pending claim 1, as amended. As for dependent claims 33 and 34, since these claims are dependent from, and thus contain all the limitations of claim 1, they are patentable for the same reasons. Accordingly, Applicants request that these grounds of rejection be withdrawn.

In view of the above amendment and remarks, allowance of claims 1, 33 and 34 is respectfully requested. A good faith effort has been made to place this application in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at (206) 622-4900 to resolve the same. Furthermore, the Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

Bernhard H. Weigl et al.

SEED Intellectual Property Law Group PLLC



Emily W. Wagner
Registration No. 50,922

EWV:cw

Enclosure:
Postcard

701 Fifth Avenue, Suite 6300
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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